



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-2167]

Heparin-Containing Medical Devices and Combination Products: Recommendations for Labeling and Safety Testing; Draft Guidance for Industry and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the draft guidance entitled “Heparin-Containing Medical Devices and Combination Products: Recommendations for Labeling and Safety Testing.” This draft guidance describes FDA’s intent to address the safety concerns by clarifying new expectations for labeling with regard to the soon-to-be revised heparin United States Pharmacopeia (USP) monographs as well as outline safety testing recommendations. This draft guidance is not final nor is it in effect at this time.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: An electronic copy of the guidance document is available for download from the Internet. See the SUPPLEMENTARY INFORMATION section for information on electronic access to the guidance. Submit written requests for single copies of the draft guidance document entitled “Heparin-Containing Medical Devices and Combination Products: Recommendations for Labeling and Safety Testing” to the Office of the Center Director, Guidance and Policy Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5431, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify comments with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Angela Krueger, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 1666, Silver Spring, MD 20993-0002, 301-796-6380.

#### SUPPLEMENTARY INFORMATION:

##### I. Background

The USP<sup>1</sup> heparin monographs have recently undergone several revisions following serious and fatal events related to the use of heparin sodium products. Investigation of heparin product overdose errors identified the expression of drug strength in the labels as a major contributing factor in these errors. This draft guidance document is intended to address these

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<sup>1</sup> USP is a scientific nonprofit organization that develops standards for the identity, strength, quality, and purity of drugs and drug ingredients marketed in the United States. These standards are published in USP’s official compendia, “United States Pharmacopeia and National Formulary.”

safety concerns by clarifying new expectations for labeling with regard to the soon-to-be revised heparin USP monographs (USP36-NF31),<sup>2</sup> as well as outline safety testing recommendations.

In addition, the outbreak of serious and often fatal events due to heparin contamination with over-sulfated chondroitin sulfate in 2008 led the USP to include in its monograph additional testing of heparin source material to ensure its quality and purity. This draft guidance also outlines use of conformance to the monograph in premarket submissions, specifically testing and documentation requirements and recommendations contained in the current USP monograph, and the guidance document “Heparin for Drug and Medical Device Use: Monitoring Crude Heparin for Quality”

(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291390.pdf>).<sup>3</sup>

## II. Significance of Guidance

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on labeling and safety testing requirements for heparin-containing medical devices and combination products. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statute and regulations.

## III. Electronic Access

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<sup>2</sup> USP monograph, USP PF 38 (3) and (5) Interim Revision Announcement, with proposed effective revision date of May 1, 2013. See also “FDA Drug Safety Communication: Important Change to Heparin Container Labels to Clearly State the Total Drug Strength” at <http://www.fda.gov/Drugs/DrugSafety/ucm330695.htm>.

<sup>3</sup> The Agency updates guidances periodically. To make sure you have the most recent version of this guidance, check the CDER guidance page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

Persons interested in obtaining a copy of the draft guidance may do so by downloading an electronic copy from the Internet. A search capability for all Center for Device and Radiological Health guidance documents is available at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>. Guidance documents are also available at <http://www.regulations.gov>. Persons unable to download an electronic copy of “Heparin-Containing Medical Devices and Combination Products: Recommendations for Labeling and Safety Testing” may send an email request to [CDRH-Guidance@fda.hhs.gov](mailto:CDRH-Guidance@fda.hhs.gov) to receive an electronic copy of the document. Please use the document number 1817 to identify the guidance you are requesting.

#### IV. Paperwork Reduction Act of 1995

This draft guidance refers to currently approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals) have been approved under OMB control number 0910-0139. The collections of information in FDA’s medical devices regulations in 21 CFR parts 801 (Labeling); 803 (Medical Device Reporting); 807, subpart E (Premarket Notification Procedures); 812 (Investigational Device Exemptions); 814, subparts A through E (Premarket Approval of Medical Devices); 814, subpart H (Humanitarian Use Devices); and 820 (Quality System Regulation) have been approved under OMB control numbers 0910-0485, 0910-0437, 0910-0120, 0910-0078, 0910-0231, 0910-0332, and 0910-0073 respectively.

#### V. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

Dated: July 2, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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